Remarks

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Support for Amendments

Support for the foregoing amendments to the claims may be found throughout the specification as originally filed, either inherently or explicitly. Specifically, support for the amendments to claims 52 and 59, and for new claims 68 and 69, may be found in the specification at page 10, lines 18-27 (particularly at lines 22-23), at page 30, lines 3-11, and in Example 9 at pages 75-77. Support for the amendments to claims 60, 62, 64 and 65 may be found in the specification at pages 41-46, and throughout the Examples. Hence, these amendments add no new matter, and their entry and consideration are respectfully requested.

II. Status of the Claims

By the foregoing amendments, claims 52, 59, 60, 62, 64 and 65 have been amended, and new claims 68 and 69 are sought to be entered. These amendments do not add new matter. Upon entry of the foregoing amendments, claims 52-69 are pending in the application, with claim 52 being the sole independent claim.

III. Summary of the Office Action

In the Office Action dated October 21, 2002, the Examiner has made one objection to claim 52, and two rejections of claims 52-67. Applicants respectfully offer the following remarks to overcome or traverse each of these elements of the Office Action.

IV. Claim Objection

In the Office Action at page 2, section 4, the Examiner has objected to claim 52 for an alleged informality, and required that the word "each" be inserted into this claim at line 4 for better grammatical form. The claim has been amended to comply with this request. Accordingly, this objection has been fully accommodated; reconsideration and withdrawal are respectfully requested.

V. Claim Rejections

A. Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 3, section 6, the Examiner has rejected claims 52-67, 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Applicants respectfully traverse this rejection.

In making this rejection, the Examiner first contends that the definition of "*in vitro*" as recited in claim 52 is vague and indefinite in light of the prior art, which is said to lack clarity itself. Additionally, the Examiner contends that the use of the term "*in vitro*" is confusing allegedly because it is used in claim 52 to refer to a reaction which takes place in an artificial environment outside of host cells, while the present specification also refers to "*in vitro*" as "a reaction done in a test tube with cells" (*see* Office Action at page 3,

section 8). Applicants respectfully disagree with these contentions, and specifically with the notion that any confusion arises from these uses of the term "*in vitro*."

Applicants respectfully remind the Examiner that an applicant may be his own lexicographer. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582, 39 USPQ2d 1573, 1576 (Fed. Cir. 1996). The Examiner also is respectfully reminded that the meaning of the term "*in vitro*," as with any term in a claim, depends on the context in which it is used. In the present case, the Examiner is apparently attempting to apply a meaning for "*in vitro*" from one context to the use of the term in a completely different context. Specifically, the portion of the specification cited above by the Examiner relates to an *in vitro* method of *selection*, as opposed to an *in vitro* method of *cloning* as is recited in the present claims. The text of the specification that describes the method of the presently claimed invention specifically describes methods of *in vitro* cloning in which the cloning reaction takes place outside of host cells (*see, e.g.*, Specification in Example 1 (particularly at page 52, lines 17-23, and page 53, line 32 to page 54, line 21); in Example 2 (particularly at page 55, line 37 to page 56, line 7); in Example 3 (particularly at page 59, lines 13-21, and at page 60, lines 30-40); in Example 4 (particularly at page 62, lines 22-30); and throughout the remaining Examples). Thus, Applicants respectfully assert that it would be abundantly clear to the ordinarily skilled artisan that an "*in vitro*" method of cloning using recombination sites refers to a method that takes place outside of host cells. This is particularly the case because the context in which the term "*in vitro*" is used in describing and claiming a *cloning method* is distinct from the context in which this term is used in the present specification (including in the passage cited by the Examiner) in referring to *selection schemes* which are not recited in the claims. Accordingly, one of ordinary skill in the art would not confuse "*in vitro*"

cloning with "*in vitro*" selection, and the term "*in vitro*" as recited in the present claims is sufficiently distinct and clear. Reconsideration and withdrawal of this portion of the rejection under 35 U.S.C. § 112, second paragraph, therefore are respectfully requested.

The Examiner next has rejected claim 52, asserting that it contains the trademark/trade name "PCR" and therefore does not comply with the requirements of 35 U.S.C. §112, second paragraph. (*See* Office Action at page 4, section 9). By the foregoing amendments, claim 52 has been amended to recite "amplification product," which conveys a clear meaning in the present context without the use of a trademark. Hence this portion of the rejection has been accommodated; reconsideration and withdrawal therefore are respectfully requested.

The Examiner next contends that claims 60, 62 and 64 are indefinite due to recitation of "mutants thereof," contending that one of ordinary skill in the art would not know how to interpret the metes and bounds of this limitation (*see* Office Action at pages 4-5, section 11). By the foregoing amendments, claims 60, 62 and 64 have been amended to recite "functional" mutants thereof. The present specification provides detailed teachings of how to prepare functional mutant recombination sites (*See, e.g.*, Specification at pages 41-44, and throughout the Examples), and discloses a substantial number of non-limiting examples of mutants of recombination sites (including nucleotide sequences thereof; *see,* e.g., Application at pages 44-46).

Accordingly, Applicants respectfully assert that one of ordinary skill could readily determine the metes and bounds of the term "functional mutants thereof" as recited in claims 60, 62 and 64, based on the guidance provided by the present specification. Claims 60, 62 and 64 therefore comport with the requirements of 35 U.S.C. §112, second paragraph.

Reconsideration and withdrawal of this portion of the rejection are therefore respectfully requested.

B. Rejection under 35 U.S.C. § 103

In the Office Action at pages 5-8, the Examiner has rejected claims 52-67 under 35 U.S.C. §103(a) as being unpatentable over Elledge *et al.* (U.S. Patent No. 5,851,808, of record as Doc. No. AB3; hereinafter "Elledge"), in view of Auerbach (U.S. Patent No. 5,354,668, of record as Doc. No. AE1; hereinafter "Auerbach"). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner has asserted that Elledge teaches an *in vitro* method of recombination between linear DNA and a host vector using a recombinase enzyme to recombine the linear DNA and a host vector to form a product vector. The Examiner also asserts that Elledge teaches the use of a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other, and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions such that recombination occurs between the first and third recombination sites and the second and fourth recombination sites thereby making a product vector. Applicants respectfully disagree with these assertions.

Independent claim 52 (and hence the remaining claims that depend therefrom) is drawn to an *in vitro* method of cloning an amplification product comprising obtaining an amplification product comprising a first recombination site and a second recombination site

which do not recombine with each other; and combining the amplification product *in vitro* with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other, under conditions such that recombination occurs between the first and third and said second and fourth recombination sites, thereby producing a product vector. Elledge does not disclose or suggest a method which comprises two recombination sites on each vector which do not recombine with each other. Hence, Elledge is seriously deficient as a primary reference upon which to attempt to base a *prima facie* case of obviousness. The disclosure of Auerbach does not cure the deficiencies in Elledge. Like Elledge, Auerbach does not disclose or suggest the use of amplification products that contain two recombination sites that do not recombine with each other.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Specifically, there must be a reason, suggestion, or motivation in the cited art that would motivate one of ordinary skill to combine the references, and that would also suggest a reasonable likelihood of success in making or using the invention as claimed as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). As noted above, neither Elledge nor Auerbach provides any disclosure or suggestion that would have motivated one of ordinary skill to have combined and/or modified their disclosures in order to make and use the

presently claimed invention. Absent such suggestion and motivation, the cited references may not be properly combined to render the claimed invention obvious. *See Fine*, 5 USPQ2d at1598.

In view of the foregoing remarks, Applicants respectfully assert that the disclosures of Elledge and Auerbach, alone or in combination, cannot support a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection of claims 52-57 under 35 U.S.C. §103 over Elledge and Auerbach therefore are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply, and allowance of all pending claims are respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the Claims:

(a) Claims 52, 59, 60, 62, 64 and 65 are sought to be amended as follows:

52. (Twice Amended) An *in vitro* method of cloning [a Polymerase Chain Reaction (PCR)] an amplification product comprising:

(a) obtaining [a PCR] an amplification product comprising a first recombination site and a second recombination site which do not recombine with each other; and

(b) combining said [PCR] amplification product *in vitro* with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other, under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a product vector.

59. (Once Amended) The method of claim 52, wherein said [PCR] amplification product is linear.

60. (Once Amended) The method of claim 52, wherein said first, second, third or fourth recombination sites are *lox* sites or functional mutants thereof.

62. (Once Amended) The method of claim 52, wherein said first, second, third or fourth recombination sites are *att* sties or functional mutants thereof.

64. (Once Amended) The method of claim 52, wherein said first, second, third or fourth recombination sites are selected from the group consisting of a *lox* site, an *att* site, an FRT site, and functional mutants thereof.

65. (Twice amended) The method of claim 52, wherein said [PCR] amplification product and said vector are combined in the presence of at least one recombination protein.

(b) New claims 68 and 69 are sought to be entered.